

encapsulated chemotherapy drug and an immunostimulating cytokine,

wherein the cytokine is encapsulated in multilamellar liposomes (MLV),

said treatment being characterized in that the subject is administered on non-consecutive days with two or more DOSES of said liposome encapsulated cytokine,

D
D a first dose being administered ^{at least three days} ~~after a time~~ ~~interval~~ following administration of said chemotherapeutic drug,

D wherein the time ~~interval~~ between administrations is such that the therapeutic effect of the combined administrations is greater than the sum of the therapeutic effects produced by administration of said chemotherapeutic drug alone and by administration of said immunostimulating cytokine alone.

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Cont. 55. (New) The method of claim 54, wherein said first dose of liposome encapsulated cytokine is administered at least three days after administration of said chemotherapeutic drug.

256. (New) The method of claim 54, wherein said cytokine is selected from the group consisting of interleukin-

2 (IL-2), IL-12, IL-15, IL-18, INF- γ , INF- α , INF- β , G-CSF, and GM-CSF.

57. (New) The method of claim 55, wherein said cytokine is selected from the group consisting of interleukins-2 (IL-2), IL-12, IL-15, IL-18, INF- γ , INF- α , INF- β , G-CSF, and GM-CSF.

³/~~58~~. (New) The method of claim ²/~~56~~, wherein said cytokine is IL-2.

59. (New) The method of claim 57, wherein said cytokine is IL-2.

⁴/~~60~~. (New) The method of claim ¹/~~54~~ wherein the liposomes comprise at least one lipid selected from the group consisting of dimyristoyl phosphatidyl choline (DMPC), dimyristoyl phosphatidyl glycerol (DMPG), 1,2-distearoyl-3-trimethylammonium propane (DSTAP), phosphatidyl choline, phosphatidyl ethanolamine and cholesterol.

61. (New) The method of claim 55 wherein the liposomes comprise at least one lipid selected from the group consisting of dimyristoyl phosphatidyl choline (DMPC), dimyristoyl phosphatidyl glycerol (DMPG), 1,2-distearoyl-3-trimethylammonium propane (DSTAP), phosphatidyl choline, phosphatidyl ethanolamine and cholesterol.

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~~5~~₆₂. (New) The method of claim ~~60~~⁴, wherein said cytokine is encapsulated in liposomes comprising (1) DMPC and (2) at least one additional lipid selected from the group consisting of dimyristoyl phosphatidyl glycerol (DMPG), and 1,2-distearoyl-3-trimethylammonium propane (DSTAP), said at least one additional lipid being in an amount of up to 50%.

63. (New) The method of claim 61, wherein said cytokine is encapsulated in liposomes comprising (1) DMPC and (2) at least one additional lipid selected from the group consisting of dimyristoyl phosphatidyl glycerol (DMPG), and 1,2-distearoyl-3-trimethylammonium propane (DSTAP), said at least one additional lipid being in an amount of up to 50%.

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~~6~~₆₄. (new) The method of claim ~~62~~⁵, wherein said liposome is composed of DMPC and DMPG.

C' Cont. [65. (New) The method of claim 63, wherein said liposome is composed of DMPC and DMPG.

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~~7~~₆₆. (New) The method of claim ~~64~~⁶, wherein the liposome comprise DMPC and DMPG in a molar ratio of about 9:1.

67. (New) The method of claim 65, wherein the liposome comprise DMPC and DMPG in a molar ratio of about 9:1.

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~~8~~₆₈. (new) The method of claim ~~54~~¹, wherein said chemotherapeutic drug is selected from the group consisting of

a chemotherapeutic anthraquinone, cisplatin, and a topoisomerase I inhibitor.

69. (new) The method of claim 55, wherein said chemotherapeutic drug is selected from the group consisting of a chemotherapeutic anthraquinone, cisplatin, and a topoisomerase I inhibitor.

9 70. (New) The method of claim 68, wherein said chemotherapeutic drug is doxorubicin (adriamycin).

71. (New) The method of claim 69, wherein said chemotherapeutic drug is doxorubicin (adriamycin).

10 72. (New) A method for antitumor therapy, comprising

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Cont.
administering to a subject in need of such treatment, a therapeutically effective amount of a chemotherapeutic drug encapsulated in liposomes and an immunostimulating cytokine encapsulated in MLV,

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D
said treatment being characterized in that the subject is administered on non-consecutive days with two or more doses of said liposome encapsulated cytokine, a first dose being administered ^{at least three days} ~~after a time interval~~ following administration of said liposome encapsulated chemotherapeutic drug, wherein the time ~~interval~~ between administration of said

liposome encapsulated chemotherapeutic drug and said liposome encapsulated cytokine is such that the combined therapeutic effect of said administrations is greater than a sum of the therapeutic effects produced by administration of the liposome encapsulated chemotherapeutic drug alone and by administration of said liposome encapsulated chemotherapeutic drug alone and by administration of said liposome encapsulated immunostimulating cytokine alone.

73. (new) The method of claim 72, wherein said liposome encapsulated cytokine is administered at least three days after administration of said liposome encapsulated chemotherapeutic drug.

11/74. (New) The method of claim 72, wherein said cytokine is selected from the group consisting of interleukin-2 (IL-2), IL-12, IL-15, IL-18, INF- γ , INF- α , INF- β , G-CSF, and GM-CSF.

75. (New) The method of claim 73, wherein said cytokine is selected from the group consisting of interleukin-2 (IL-2), IL-12, IL-15, IL-18, INF- γ , INF- α , INF- β , G-CSF, and GM-CSF.

12/76. (New) The method of claim 74, wherein said cytokine is IL-2.

77. (New) The method of claim 75, wherein said cytokine is IL-2.

¹³ 78. (New) The method of claim ¹⁰ 72 wherein the liposomes encapsulating said immunostimulating cytokine comprise at least one lipid selected from the group consisting DMPC, DMPG, DSTAP, phosphatidyl choline, phosphatidyl ethanolamine and cholesterol.

79. (New) The method of claim 73 wherein the liposomes encapsulating said immunostimulating cytokine comprise at least one lipid selected from the group consisting DMPC, DMPG, DSTAP, phosphatidyl choline, phosphatidyl ethanolamine and cholesterol.

¹⁴ 80. (new) The method of claim ¹³ 78, wherein said cytokine is encapsulated in liposomes comprising (1) DMPC and (2) at least one additional lipid selected from the group consisting of DMPG and DSTAP, said at least one additional lipid being in an amount of up to 50%.

81. (new) The method of claim 79, wherein said cytokine is encapsulated in liposomes comprising (1) DMPC and (2) at least one additional lipid selected from the group consisting of DMPG and DSTAP, said at least one additional lipid being in an amount of up to 50%.

¹⁵ 82. (New) The method of claim ¹⁴ 80, wherein said liposome comprise of DMPC and DMPG.

83. (New) The method of claim 81, wherein said liposome comprises of DMPC and DMPG.

¹⁶ 84. (new) The method of claim ¹⁵ 82, wherein the liposome DMPC and DMPG are present in a molar ratio of about 9:1.

85. (new) The method of claim 83, wherein the liposome DMPC and DMPG are present in a molar ratio of about 9:1.

¹⁷ 86. (new) The method of claim ¹⁰ 72, wherein the liposomes encapsulating said chemotherapeutic drug comprise 1-10 mole percent of a lipid having a polar head group derivatized with a polyethylene glycol (PEG) chain which has a molecular weight of between 750 and 10,000 dalton.

87. (new) The method of claim 73, wherein the liposomes encapsulating said chemotherapeutic drug comprise 1-10 mole percent of a lipid having a polar head group derivatized with a polyethylene glycol (PEG) chain which has a molecular weight of between 750 and 10,000 dalton.

¹⁸ 88. (New) The method of claim ¹⁰ 72, wherein said chemotherapeutic drug is selected from the group consisting of

a chemotherapeutic anthraquinone, cisplatin, and a topoisomerase I inhibitor.

89. (New) The method of claim 73, wherein said chemotherapeutic drug is selected from the group consisting of a chemotherapeutic anthraquinone, cisplatin, and a topoisomerase I inhibitor.

19/ 90. (new) The method of claim 88, wherein said chemotherapeutic drug is doxorubicin (adriamycin).

91. (new) The method of claim 89, wherein said chemotherapeutic drug is doxorubicin (adriamycin).

20/ 92. (new) The method of claim 90, wherein said chemotherapeutic drug is polyethylene glycol-coated liposomal doxorubicin.

93. (new) The method of claim 91, wherein said chemotherapeutic drug is polyethylene glycol-coated liposomal doxorubicin.

REMARKS

The Official Action of October 4, 2001, and the prior art cited and relied upon therein have been carefully reviewed. The claims in the application are now claims 54-93, and these claims define patentable subject matter warranting